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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/807,811	03/24/2004	Ian R. Scott	MPG0401(S)	4379

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Michael P. Aronson
MP&G Aronson Inc.
2 Mandarin Lane
West Nyack, NY 10994

EXAMINER	
MILLER, MARINA I	

ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 11/17/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/807,811	SCOTT, IAN R.	
	Examiner	Art Unit	
	Marina Miller	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 September 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-48* is/are pending in the application.

4a) Of the above claim(s) *3,7-14,16,18-23 and 28-48* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4-6,15,17 and 24-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4/30/04;5/5/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's election without traverse of Group I (claims 1-27) in the reply filed 9/5/2006 is acknowledged.

Applicant also elected the following species:

Species A: the CTFA Dictionary of claim 4;

Species B: retinol and retinol boosters as a pair of actives of claim 6;

Species C: a high-throughput assay being the resolution or prevention of acne of claim 15; and

Species D: IL-1 hypercornification of claim 17.

Claims 1-48 are pending.

Claims 3, 7-14, 16, 18-23, 28-48 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected inventions and species, there being no allowable generic or linking claims.

An action on the merits of claims 1-2, 4-6, 15, 17, and 24-27, as they read on the elected species, follows.

Priority

Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date, the U.S. provisional applications 60/457,859 filed 3/26/2003; 60/457,860 filed 3/26/2003; 60/457,861 filed 3/26/2003, and 60/483,564 filed 6/28/2003 for claims 115 and 17. Claims 15 and 17 are drawn to a method comprising an assay predictive of the resolution or prevention of acne and the IL1-induced hypercornification assay. The resolution or prevention of acne using the IL1-induced hypercornification assay is not supported by the provisional

applications listed above.

If applicant desires benefit of these provisional applications, applicant is invited to point to specific support by page and line number for each limitation of instant claims in the provisional applications mentioned above. Priority for claims 15 and 17 is granted only to the filing date of the instant application filed 3/24/2004.

Information Disclosure Statement

The information disclosure statements ("IDS") filed 4/30/2004 and 5/5/2004 have been considered in full.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentations is "undue." These factors include, but are not limited to:

a) The breadth of the claims;
b) The nature of the invention;
c) The state of the prior art;
d) The level of one of ordinary skill;
e) The level of predictability in the art;
f) The amount of direction provided by the inventor;
g) The existing of working examples; and
h) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

In re Wands, 858 F.2d 731, 737 (Fed. Cir. 1988).

The Board also stated that although the level of skill in molecular biology is high, the results of experiments in genetic engineering are unpredictable. 858 F.2d at 740. While all of these factors are considered, sufficient amount for a prima facie case are discussed below.

Claims 15-17 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

a) Claim 15 recites the limitation "resolution" of acne. The instant specification does not define or disclose what is intended as "resolution." The Free Dictionary OnLine defines "resolution of disease" as "[t]he subsiding or termination of an abnormal condition, such as a fever or an inflammation" at http://medical-dictionary.thefreedictionary.com/resolution (2 pages) accessed 11/9/2006; see also Harrison, *Br. J. Rheumatol.*, 35:1096-1100, at 1099 (1996) (disclosing that resolution [opposing to remission] implies complete arrest of the disease process akin to a "cure"). Therefore, "resolution" is broadly interpreted to encompass both "ameliorating" and "curing." While claims 15 and 17 are enabled for "ameliorating" acne, claims 15 and 17 are not enabled for "curing" acne.

The claims are narrow because they are directed to a method for identifying highly synergistic combinations of biologically active agents that target resolution of acne by using the inhibition of IL1-induced hypercornification assay. The instant specification does not provide specific guidance to practice the invention because it does not disclose how to predict "prevention" or curing of acne.

The instant specification does not provide specific guidance to practice the invention because it does not disclose how to predict "prevention" of acne in the assay which necessarily uses acne tissues. One cannot "predict" that disease would not commence based on the results of the assay conducted on already "diseased" cells without undue experimentation.

b) The invention is drawn to a method for identifying highly synergistic combinations of biologically active agents.

c, e) A review of the prior art shows that anti-inflammatory compounds ameliorate acne. *See* Eady, *Br. J. Dermatol.*, 131(1):331-336 (1994); Eady, *J. Invest. Dermatol.*, 101:86-91 (1993). The review has further shown that different types of anti-inflammatory therapy is effective for reducing acne. *See* Zouboulis, *Dermatol.*, 203(4):277-279 (2001); Zouboulis, *JEADV*, 15, Suppl. 3:63-67 (2001). The review has also shown that synergistic combinations of therapeutic compounds for treating acne may be identified by using the IL1 hypercornificaiton assay and a systemic discovery method. See Zouboulis, *JEADV*, 15, Suppl. 3:63-67 (2001); Zouboulis, *Dermatol.*, 203(4):277-279 (2001); Borisy, *PNAS*, 100(13):7977-7982 (June 24, 2003); Guy, *J. Invest. Dermatol.*, 110:410-415 (1998). The prior art does not disclose how to predict prevention of acne from an assay using acne tissue. The prior art does not disclose how to predict "curing" (*i.e.*, complete arrest) of acne.

d) The skill of those in the art of molecular biology is high.

f) The specification does not provide any working examples demonstrating identifying a combination of compounds that will cure or prevent an onset of acne. In fact, the specification only discloses a general outline of the IL1 and a simulated follicle *P. Acnes* assay unrelated to

any experiments and does not teach how to predict prevention of acne from the conducted assay or to predict curing of acne.

h) In order to practice the claimed invention, one skilled in the art must randomly select parameters correlating the result of the assay and an onset or termination of acne and must guess which result to use for predicting cure or prevention of acne. This constitutes undue experimentation.

Due to the undue experimentation required to obtain the goal of the invention, the lack of directions presented in the specification, the complex nature of the invention, and the state of the prior art showing only identifying synergistic compositions of compounds for ameliorating acne, the specification fails to teach one skilled in the art how to use the claimed method for predicting prevention of acne.

Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-2, 4-6, 15, 17, and 24-27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 4-6 recites a "library of potential *actives*." It is not clear what "actives" are intended, *e.g.*, a library of biologically active compounds, a library of activities *per se* (*e.g.*, promotion of hair growth, resolution of acne, *etc.*), or some other limitation. As the intended limitation is not clear, claims are 1-2, 4-6, 15, 17, and 24-27 are indefinite.

Claim 1 recites in step (ii) "identifying a subset of components by testing each component for activity in a Multi-Pathway High Throughput Assay that targets a biological end effect." It is not clear whether the "activity" OR the Assay targets a biological end effect. It is also unclear whether all components of the library exhibit one know activity towards one biological effect or multiple known activities toward one/multiple biological effects. As the intended limitation is not clear, claims are 1-2, 4-6, 15, 17, and 24-27 are indefinite.

Claim 1 recites the limitation an "Assay … has a known useful range of detectability." It is not clear what range is intended by "useful." It is also unclear whether a "range of detectability" is intended to mean, for example, a range of a specific activity where the activity may be detected within preselected error (or above a preselected threshold), a level of activity above which a particular assay may detect the activity (*i.e.*, assay limitations), a range of different activities which may be detected by the same assay, *etc*. As the intended limitation, and the intended metes and bounds of the claim are not clear, claims are 1-2, 4-6, 15, 17, and 24-27 are indefinite.

Claim 1 recites in step (iii) the limitation "the concentration … is adjusted using a Single Component Scaling Protocol such that its activity is scaled." It is not clear whether "adjusting", "using a Protocol", and "scaling" activity are intended to be active, positive steps of the method. It is further unclear what specific steps of "adjusting", "using a Protocol," and "scaling activity," are intended. As the intended limitation is not clear, claims are 1-2, 4-6, 15, 17, and 24-27 are indefinite.

Claim 1 recites in step (iii) the limitation the "activity reliably detectable at … the useful range of the … Assay." The criteria of the "reliability" of detection are not clear. Further, the

meaning of the limitation "useful range of the assay" is also unclear because the criteria of "usefulness" are unclear. Also, it is unclear what "range of the assay" is intended and neither the specification nor the claims clarifies/defines the limitation. As the intended limitation is not clear, claims are 1-2, 4-6, 15, 17, and 24-27 are indefinite.

Claim 15 recites the limitation "wherein the ... assay is predictive of the resolution or prevention of acne." It is not clear whether the limitation "is predictive" is intended to limit the method steps of the assay/data. If the former, then the claims should be to rewritten using active, positive language. If the latter, then it is not clear what further limitation of data used in the claimed method is intended by the methods of measuring the data. As the intended limitation is not clear, claims 15 and 17 are indefinite.

Claim 17 limits claim 1 to a specific assay, *i.e.*, the inhibition IL1-induced hypercornification assay. The assay "comprises" pieces of epidermis and "using" a medium, embedding skin pieces, sectioning the assembly, and histology to be "carried out". It is not clear what further limitation of the method of claim 1 is intended and whether the limitations recited in claim 17 are intended to limit the method steps, assay, or data obtained by the assay/method. It is not clear whether using, embedding, sectioning, and carrying out are intended to be active, positive method steps or merely an intended use of the method. As the intended limitations are not clear, claim 17 is indefinite.

Claim 17 recites the limitation "test samples." It is not clear whether "test samples" are intended to mean samples comprising compounds (or mixtures thereof) from a library of active compounds being tested or some other samples. As the intended limitation is not clear, claim 17 is indefinite.

Claim 17 recites the limitation "the entire assembly." The antecedent basis of the limitation is uncle because the claim does not recite "an entire assembly," it only recites "a multiple well assembly." As the intended limitation is not clear, claim 17 is indefinite.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-2 and 27 are rejected under 35 U.S.C. 102(b) as being anticipated by Stockwell, US 2002/0019011.

Stockwell discloses a method for identifying synergistic combinations of therapeutics using steps of selecting a library [0038]-[0046], identifying a subset of compounds which display significant activity by testing the library in a variety of high throughput assays that targets a biological effect [0048]-[0079], and identifying a binary (or N component) mixture of synergistic compounds [0038], [0108]-[0113], examples 1 and 2 on p. 10-12, claims 1-2. Stockwell discloses adjusting concentration of compounds ([0107]-[0108], examples 1-2). Thus, Stockwell anticipates claims 1-2 and 27.

Claims 1-2 and 24-26 are rejected under 35 U.S.C. 102(a) as being anticipated by Borisy, US 2002/0165261.

Borisy discloses a method for identifying a synergistic combination of drugs (abstract). Borisy discloses selecting a library of active compounds (see pages 6-11), identifying a subset of compounds active to a biological effect using a high throughput assay, and identifying sinegristic mixtures of the compounds (examples 2-3). Borisy discloses adjusting concentration of compounds (example 1-3; tables 1-5). Thus, Borisy anticipates claims 1-2. Borisy discloses adjusting concentration and lambda factor being less than or equal to 0.4, 0.2, and 0.1 (see tables 1-4), thereby anticipating claims 24-26.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 4-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stockwell, US 2002/0019011, as applied to claims 1-2 and 27 above, in view of Granger, WO 02/02074, and further in view of the CTFA Dictionary, retrieved from http://www.ctfa-buyersguide.org/pls/ctfa/ctfa_bg.bg.list_ingred?p_searchtype=&p_ingred_... accessed 11/3/2006.

Stockwell teaches the method of claims 1-2 and 27, as set forth above.

Stockwell does not teach the CTFA Dictionary, retinol, and retinol boosters.

Granger discloses testing retinol and various retinol boosters for treating multiple skin conditions p. 1-2, 4-6, wherein retinol is a compound selected from the CTFA Dictionary (see the CTFA Dictionary).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to modify the method of Stockwell to use retinol and retinol boosters for treating skin diseases, such as taught by Granger, where the motivation would have been to use a well-known anti-inflammatory activity of retinol and improve conversion of retinol to retinoic acid by using boosters providing synergistic effect for treating skin, as taught by Granger, p. 1-4.

Claims 15 and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stockwell, US 2002/0019011, as applied to claims 1-2 and 27 above, in view of Guy, *J. Invest. Dermatology*, 110:410-415 (1998), and further in view of Zouboulis, JEADV, 15, Suppl. 3:63-67 (2001).

Stockwell teaches the method of claims 1-2 and 27, as set forth above.

Stockwell does not teach a multi-pathway high throughput assay and IL1-induced hypercornificaiton assay.

Guy discloses the IL1-induced hypercornificaiton assay using skin tissue (p. 410-411). Guy discloses using a culture mediun containing a level of IL1 sufficient to cause hypercornificaiton (p. 411). Guy discloses histological sectioning and immunohistochemistry (p. 411).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to modify the method of Stockwell to use the IL1-induced hypercornificaiton assay for

acne tissue/cells, such as taught by Granger, where the motivation would have been to use pro-inflammatory cytokines that induce early cornificaiton of skin cells for identifying anti-inflammatory regimens in the treatment of acne, as taught by Zouboulis, p. 65.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marina Miller whose telephone number is (571)272-6101. The examiner can normally be reached on 8-6, M-Thu.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang, Ph. D. can be reached on (571)272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Marjorie A. Moran
11/12/06
MARJORIE A. MORAN
PRIMARY EXAMINER

Marina Miller
Examiner
Art Unit 1631